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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/303,232	04/30/99	ADAMCZEWSKI M	MO-5176/LEA3

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EXAMINER	
SCHNIZER, R	
ART UNIT	**PAPER NUMBER**
1632	18

DATE MAILED: 11/08/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE COPY

Office Action Summary	Application No. 09/303,232	Applicant(s) Adamcz wski et al
	Examiner Richard Schniz r	Group Art Unit 1632

☒ Responsive to communication(s) filed on *Aug 3, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-20 and 22-33* is/are pending in the applicat

Of the above, claim(s) *8, 9, 11-16, 18-20, 32, and 33* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 10, 17, and 22-31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *12*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

An amendment and a supplemental information disclosure statement were received and entered as Paper Nos. 11 and 12, respectively, on 8/3/00. Applicant's election without traverse of group I, claims 1-7, 10, 17, and 22-31 in Paper No. 11 is acknowledged, and these claims are under consideration in the following office action.

Rejections Withdrawn.

The rejection in paper No. 8 of claims 1-7, 10, 17, and 22-31 under 35 U.S.C. 101 is withdrawn in view of Applicant's amendment.

The rejections in Paper No. 8 of claims 1-7, 10, 17, and 22-31 under 35 U.S.C. 112, second paragraph are withdrawn in view of Applicant's amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 10, 17, and 22-31 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid which comprises a sequence selected from the sequences according to SEQ ID NOS: 1, 3, or 5, and partial sequences at least

14 base pairs in length of the sequences according to SEQ ID NOS: 1, 3, or 5, as are known in the art (Celniker et al, 1998; Liao et al, 1998; and Vogel et al, 1998), and sequences which exhibit at least 70% identity between position 1295 and positions 2195 from SEQ ID NO: 1, or between position 432 and position 1318 from SEQ ID NO: 3, or between position 154 and position 1123 of SEQ ID NO: 5, does not reasonably provide enablement for any and all partial sequences which are at least 14 base pairs in length of the sequences according to SEQ ID NOS: 1, 3, or 5, or any and all sequences which exhibit at least 70% identity between position 1295 and positions 2195 from SEQ ID NO: 1, or between position 432 and position 1318 from SEQ ID NO: 3, or between position 154 and position 1123 of SEQ ID NO: 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons of record in Paper No. 8.

The claimed invention encompasses nucleic acids which encode a complete or partial insect acetylcholine receptor (AchR). In one embodiment the nucleic acid need only comprise 14 base pairs from SEQ ID NO: 1, 3, or 5. In another embodiment, the nucleic acid must hybridize with SEQ ID NO: 1, 3, or 5 in 2X SSC at 60°C. In a third embodiment, the claimed nucleic acids must be 70% identical to a specified fragment of SEQ ID NO: 1, 3, or 5. The claimed nucleic acids are asserted to be useful for discovering insecticides. See page 6, line 28 to page 7, line 6. It is reasonable to assume that this process requires expression of the polypeptides encoded by the

claimed nucleic acids, and the ability to analyze some function of the expressed polypeptides. For this reason the utility of the nucleic acids depends upon the function of the encoded polypeptide.

The scope of the claimed invention is very broad. The first embodiment encompasses at least 5000 different 14-base pair nucleic acids, as well as many thousand more nucleic acids of longer lengths. The second and third embodiments clearly encompass nucleic acids which encode truncated polypeptides, polypeptides comprising a variety missense mutations, and combinations of the two. For example, the genus of nucleic acids which are only 70% identical to a portion of SEQ ID NO:1 includes species in which sequence differences occur only in the first base of each codon. These species could encode a polypeptide of only about 10% sequence identity to the corresponding segment of SEQ ID NO:1. Thus the scope of this embodiment encompasses sequences encoding polypeptides which range from about 10% identical to the recited sequence fragments to those which are 100% identical to the recited fragments.

The specification fails to teach which of the claimed nucleic acids encode a polypeptide which can be used as intended, *i.e.* to screen for pesticides, and for the reasons discussed in Paper NO. 8, one of skill in the art cannot currently predict which of the claimed polynucleotides can be used as intended. For these reasons, it would require undue experimentation to make or use the invention commensurate in scope with the claims.

Response to Arguments

Applicant's arguments filed 8/3/00 have been fully considered but they are not persuasive.

Applicant argues that the ability of a sequence to encode an AchR can be determined simply by comparisons to known sequences. This is unpersuasive in light of references cited in Paper No. 8 (Bowie et al, Ngo et al, and Frommel et al) which set forth the state of the art regarding the prediction of protein activities from amino acid sequences. Briefly, this is an extremely unpredictable art in which the effects of amino acid substitution in even well-known proteins cannot be predicted with certainty. Thus it is unclear which amino acid substitutions would render a polypeptide non-functional, and so it is unclear which of the claimed polynucleotides would encode some function associated with acetylcholine receptors. In such situations guidance and exemplification in the specification are warranted. In this case there is no guidance which would allow one to predict which nucleic acids could be used as intended. The only example provided in the specification describes the expression in eukaryotic cells of an undisclosed nucleic acid which appears to form a homooligomeric nicotinic AchR. Clearly, none of the claimed 14 base pair nucleic acids could be expected to be useful in such an assay because they cannot encode a polypeptide which is sufficiently long to form a transmembrane channel. However, the specification teaches no other means of screening these nucleic acids for function. Applicant argues that there is no need to teach what is well known in the art, but offers no evidence that the prediction of protein function from amino acid sequence is routine, whereas the previous office action cited references (Bowie et al, Ngo et al, and Frommel et al) which indicated that such predictions are not routine in the art. Because Applicant has failed to show how to determine which of the claimed nucleic acids can be used as intended, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 10, 17, and 22-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 10, 17, and 22-31 are indefinite because it is unclear what is intended by the phrase "partial acetylcholine receptor". Specifically it is unclear what criteria are involved in establishing whether a polypeptide is a partial acetylcholine receptor or not. Is there a functional requirement? If so, is it ligand binding, channel activity, response to agonists or antagonists, or some combination of these? Is immunological cross-reactivity sufficient to identify a polypeptide as a partial AchR? The specification does not appear to provide any criteria for determining what constitutes a partial AchR, thus one of skill in the art is not apprised of the metes and bounds of the claims.

Claim 17 is also indefinite because it recites "[t]he regulatory sequence of claim 3" and "the nucleic acid" without antecedent basis. Claim 17 is ultimately dependent on claim 1, and encompasses all of the nucleic acids recited by Claim 1. It is unclear which single nucleic acid is referred to by claim 17 as "the nucleic acid". Claim 17 is also drawn to the natural regulatory sequence of the nucleic acid sequence recited in claim 1. Claim 1 recites at least three cDNAs

which appear to be the products of different genes. Thus, It is unclear which regulatory sequence is intended to be "[the] regulatory sequence of claim 3".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 stands rejected under 35 U.S.C. 102(a) as being anticipated by Schulte (1999) for the reasons of record in paper No. 8.

Schulte teaches GenBank Accession No. AF143486 which is 97.8% identical to SEQ ID NO:1, and is 100% identical to SEQ ID NO:3 between positions 432 and 1318.

Schulte teaches GenBank Accession No. AF143847 which is 9734% identical to SEQ ID NO: 5, and is 100% identical to SEQ ID NO:5 between postions 154 and 1123.

Thus Schulte anticipates the claim.

Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Celniker (1998) , or Liao (1998), or Vogel (1998) for the reasons of record in paper No. 8.

Celniker teaches GenBank Accession No. AC004326, which teaches nucleotides 34085-34912 of P1 clone DS05899, which is 99.4% identical to bases 9-836 of SEQ ID NO:1. In particular Celniker teaches bases 34085-34438 which are identical to 340 bases from 496 to 836 of SEQ ID NO:1.

Liao et al teach GenBank Accession No. AF045432 which identical to SEQ ID NO: 3 over a length of 79 bases.

Vogel et al teach GenBank Accession No. Z97178 which is identical to SEQ ID NO: 5 over a length of 98 bases.

Thus Celniker, Liao and Vogel each anticipate the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-7 and 24-31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Schulte, Celniker, or Liao, or Vogel, in view of Ausubel et al (for the reasons of record in paper No. 8.

Schulte teaches GenBank Accession No. AF143486 which is 97.8% identical to SEQ ID NO:1, and is 100% identical to SEQ ID NO:3 between postions 432 and 1318.

Schulte teaches GenBank Accession No. AF143847 which is 9734% identical to SEQ ID NO: 5, and is 100% identical to SEQ ID NO:5 between postions 154 and 1123.

Celniker teaches GenBank Accession No. AC004326, which teaches nucleotides 34085-34912 of P1 clone DS05899, which is 99.4% identical to bases 9-836 of SEQ ID NO:1. In particular Celniker teaches bases 34085-34438 which are identical to 340 bases from 496 to 836 of SEQ ID NO:1.

Liao et al teach GenBank Accession No. AF045432 which identical to SEQ ID NO: 3 over a length of 79 bases.

Vogel et al teach GenBank Accession No. Z97178 which is identical to SEQ ID NO: 5 over a length of 98 bases.

None of these references teaches vectors or host cells comprising the nucleic acids of the invention.

Ausubel teaches the introduction of nucleic acids into host cells and the use of vectors to do so.

It would have been obvious to one of ordinary skill in the art at the time of the invention to insert the nucleic acids of Schulte, Celniker, Liao, or Vogel into vectors, and to subsequently transform host cells as taught by Ausubel. One would have been motivated to do so in order to

express the encoded polypeptides for biochemical characterization. See page 9-1, first paragraph.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 8/3/00 have been fully considered but they are not persuasive.

Applicant argues that Schulte does not constitutes prior art because the specification has been amended to claim priority to German Application 19819829.9, filed 5/4/98. The corresponding priority document is present in the file, but the rejection will be maintained until a translation is filed with the office.

Applicant argues that Celniker, Liao, and Vogel do not anticipate claim 1, or render obvious claims 2-7 and 24-31, because they do not teach each and every element of the claimed invention. Specifically, Applicant asserts that the sequence of Celniker reference lacks any statement of functionality for the disclosed nucleic acid, and asserts that neither Celniker, Liao nor Vogel teaches Applicant's entire sequence.

This is unpersuasive because the claim does not recite any functionality, and it does not require Applicant's entire sequence. The claim is drawn to a nucleic acid encoding a complete **or** partial insect acetylcholine receptor. Applicant describes SEQ ID NOS 1, 3, and 5 as encoding AchR subunits, therefore any fragment of SEQ ID NOS; 1, 3, or 5 encodes a partial insect AchR. Celniker, Liao, and Vogel each teach nucleic acids which are identical to a portion of an insect

AchR over a length of greater than 14 bases as required by the claim. The elements of the claim are set forth in a Markush format wherein the claimed genus is set forth as species denoted (a), (b), (c), (d), (e), and (f). The cited art clearly anticipates, and renders obvious, species (b) which is drawn to nucleic acids at least 14 nucleotides in length. The rejections under 35 U.S.C. 102 and 103 are proper because the prior art anticipates, or renders obvious, at least one species of the genus described by the Markush group. A generic claim cannot be allowed if the prior art discloses species falling within the claimed genus. See MPEP 2131.02. Furthermore, Applicant has failed to provide any evidence that the entire sequence of Celniker does not encode an insect AchR. Applicant's assertion that the sequence of Celniker may encode a transmembrane domain which is "ubiquitous to every membrane-bound protein in a fruit fly" is not supported by evidence, and the existence of any domain which is identically conserved among fruit fly membrane proteins is highly unlikely in view of the fact that the PTO database search detected the sequence of Celniker only once.

Because the Applicant's arguments are based on limitations which are not recited in the claims, the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

This application contains claims 8, 9, 11-16, 18-20, 32, and 33 drawn to an invention nonelected with traverse in Paper No. 11. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached on Mondays and Thursdays between the hours of 6:20 AM and 3:50 PM, and on Tuesdays, Wednesdays and Fridays between the hours of 7:00 AM and 4:30 PM (Eastern time). The examiner is off every other Friday, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. The FAX phone numbers for art unit 1632 are 703-308-4242 and 703-305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Karen M. Hauda

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Richard Schnizer, Ph. D.